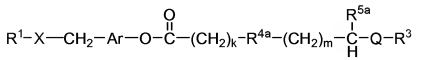
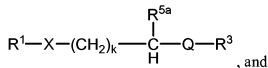
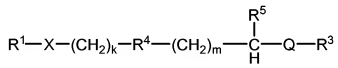
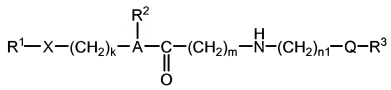


This listing of the claims replaces any and all prior versions and listings of claims in the application:

# **LISTING OF THE CLAIMS**

1. (Currently amended) A composition comprising a biologically active compound, a transport moiety and a self-immolating linker moiety linking the biologically active compound and the transport moiety, wherein the transport moiety comprises a structure selected from the group consisting of  $(ZY)_nZ$ ,  $(ZYZ)_nZ$ ,  $(ZYY)_nZ$ , and  $(ZYYY)_nZ$ , wherein each Z is L-arginine or D-arginine, and each Y is independently an amino acid that does not comprise an amidino or guanidino moiety, and wherein n is an integer of from 2 to 10, wherein the conjugate has a structure selected from



wherein

R<sup>1</sup> is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

A is N or CH;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;

R<sup>2</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>3</sup> is the transport moiety;

R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

R<sup>4a</sup> is S, O, NR<sup>6</sup> or CR<sup>7a</sup>R<sup>8a</sup>;

R<sup>5</sup> is OH, SH, NHR<sup>6</sup>, or -CONH<sub>2</sub>;

R<sup>5a</sup> is H, OH, SH, NHR<sup>6</sup>, or -CONH<sub>2</sub>;

R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen, alkyl or arylalkyl; and

R<sup>7a</sup> and R<sup>8a</sup> are independently hydrogen or alkyl; and

k and m are independently either 1 or 2; and

n1 is an integer of from 1 to 10.

2. (original) The composition according to claim 1, wherein each Y is independently selected from the group consisting of alanine, cysteine, aspartic acid, glutamic acid, phenylalanine, glycine, histidine, isoleucine, lysine, leucine, methionine, asparagine, proline, glutamine, serine, threonine, valine, tryptophan, hydroxyproline, tyrosine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine, sarcosine and  $\epsilon$ -amino caproic acid.

3. (Original) The composition according to claim 1, wherein the transport moiety comprises the structure (ZYZ)<sub>n</sub>Z, and wherein n is an integer ranging from 2 to 5.

4. (previously presented) The composition according to claim 1, wherein the transport moiety comprises the structure (ZY)<sub>n</sub>Z and wherein n is an integer ranging from 4 to 10.

5. (Original) The composition according to claim 1, wherein the transport moiety comprises the structure (ZYY)<sub>n</sub>Z, and wherein n is an integer ranging from 4 to 10.

6. (Original) The composition according to claim 1, wherein the transport moiety comprises the structure  $(ZYYY)_nZ$ , and wherein n is an integer ranging from 4 to 10.

7. Canceled

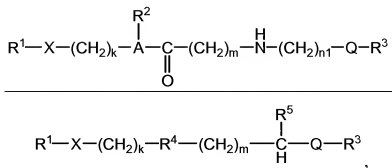
8. (original) The composition according to claim 1, wherein Y is a gene-encoded amino acid.

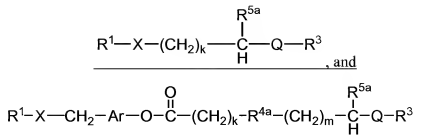
9. (Original) The composition according to claim 1, wherein Y is an amino acid other than a gene-encoded amino acid.

10. (Original) The composition according to claim 3, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 3 or 4.

11. (Currently amended) A composition, comprising:  
 a biologically active compound, a transport moiety and a self-immolating linker moiety linking the biologically active compound and the transport moiety,  
 wherein the transport moiety comprises a structure selected from the group consisting of  $(ZY)_nZ$ ,  $(YZ)_nZ$ ,  $(ZYY)_nZ$ , and  $(ZYYY)_nZ$ ,

each Z is L-arginine or D-arginine, each Y is independently glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine or  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8, wherein the conjugate has a structure selected from





wherein

R<sup>1</sup> is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

A is N or CH;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;

R<sup>2</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>3</sup> is the transport moiety;

R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

R<sup>4a</sup> is S, O, NR<sup>6</sup> or CR<sup>7a</sup>R<sup>8a</sup>;

R<sup>5</sup> is OH, SH, NHR<sup>6</sup>, or -CONH<sub>2</sub>;

R<sup>5a</sup> is H, OH, SH, NHR<sup>6</sup>, or -CONH<sub>2</sub>;

R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen, alkyl or arylalkyl; and

R<sup>7a</sup> and R<sup>8a</sup> are independently hydrogen or alkyl; and

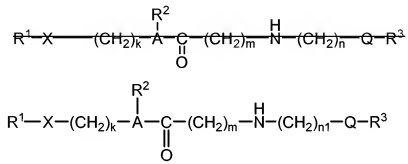
k and m are independently either 1 or 2; and

n1 is an integer of from 1 to 10.

12. (Original) The composition according to claim 5, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8.

13. (Original) The composition according to claim 6, wherein each Y is independently selected from the group consisting of glycine,  $\gamma$ -amino butyric acid,  $\beta$ -alanine and  $\epsilon$ -amino caproic acid, and n is 6, 7 or 8.

14. (Currently amended) The composition according to claim 1, wherein the conjugate has the following structure:



wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^2$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^2$ ;

A is N or CH;

$\text{R}^2$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

$\text{R}^3$  is the transport moiety;

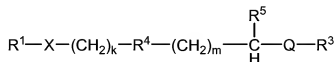
k and m are independently either 1 or 2; and

n is an integer of from 1 to 10.

15. (Original) The composition according to claim 14, wherein each of X and Q is independently selected from the group consisting of  $\text{---C(O)O---}$ ,  $\text{---O-C(O)---}$ ,  $\text{---C(O)NH---}$ ,  $\text{---NH-C(O)---}$ ,  $\text{---OC(O)NH---}$ ,  $\text{---S-S---}$ ,  $\text{---C(S)O---}$ ,  $\text{---C(S)NH---}$ ,  $\text{---NHC(O)NH---}$ ,  $\text{---SO}_2\text{NH---}$ ,  $\text{---SONH---}$ , phosphate, phosphonate and phosphinate.

16. (Original) The composition according to claim 14, wherein each of X and Q is independently selected from the group consisting of -C(O)O-, -O-C(O)-, -C(O)NH-, -NH-C(O)-, -OC(O)NH- and -NHC(O)NH-.

17. (Currently amended) The composition according to claim 1, wherein the conjugate has the following structure:



wherein:

$R^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $R^1$  and  $R^2$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $R^1$  and  $R^2$ ;

$R^2$  is the transport moiety;

$R^4$  is S, O,  $NR^6$  or  $CR^7R^8$ ;

$R^5$  is OH,  $SH$ ,  $NHR^6$  or  $CONH_2$ ;

$R^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

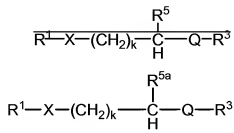
$R^7$  and  $R^8$  are independently hydrogen, alkyl or arylalkyl; and

k and m are independently either 1 or 2.

18. (Original) The composition according to claim 17 wherein each of X and Q is independently selected from the group consisting of -C(O)O-, -O-C(O)-, -C(O)NH-, -NH-C(O)-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate and phosphinate.

19. (Original) The composition according to claim 17, wherein each of X and Q is independently selected from the group consisting of -C(O)O-, -O-C(O)-, -C(O)NH-, -NH-C(O)-, -OC(O)NH- and -NHC(O)NH-.

20. (Currently amended) The composition according to claim 1, wherein the conjugate has the following structure:



wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

$\text{R}^3$  is the transport moiety;

$\text{R}^5$  is H, OH, SH,  $\text{NHR}^6$ , or  $\text{CONH}_2$ ;

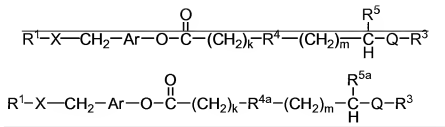
$\text{R}^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

k is 1 or 2.

21. (Original) The composition according to claim 20, wherein each of X and Q is independently selected from the group consisting of  $\text{-C(O)O-}$ ,  $\text{-O-C(O)-}$ ,  $\text{-C(O)NH-}$ ,  $\text{-NH-C(O)-}$ ,  $\text{-OC(O)NH-}$ ,  $\text{-S-S-}$ ,  $\text{-C(S)O-}$ ,  $\text{-C(S)NH-}$ ,  $\text{-NHC(O)NH-}$ ,  $\text{-SO}_2\text{NH-}$ ,  $\text{-SONH-}$ , phosphate, phosphonate and phosphinate.

22. (Original) The composition according to claim 20, wherein each of X and Q is independently selected from the group consisting of  $\text{-C(O)O-}$ ,  $\text{-O-C(O)-}$ ,  $\text{-C(O)NH-}$ ,  $\text{-NH-C(O)-}$ ,  $\text{-OC(O)NH-}$  and  $\text{-NHC(O)NH-}$ .

23. (Currently amended) The composition according to claim 1, wherein the conjugate has the following structure:



wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;

$\text{R}^2$  is the transport moiety;

$\text{R}^4$  is S, O,  $\text{NR}^6$  or  $\text{CR}^7\text{R}^8$ ;

$\text{R}^5$  is H, OH, SH,  $\text{CONHR}^6$  or  $\text{NHR}^6$ ;

$\text{R}^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

$\text{R}^7$  and  $\text{R}^8$  are independently hydrogen or alkyl; and,

k and m are independently either 1 or 2.

24. (Original) The composition according to claim 23, wherein each of X and Q is independently selected from the group consisting of -C(O)O-, -O-C(O)-, -C(O)NH-, -NH-C(O)-, -OC(O)NH-, -S-S-, -C(S)O-, -C(S)NH-, -NHC(O)NH-, -SO<sub>2</sub>NH-, -SONH-, phosphate, phosphonate and phosphinate.

25. (Original) The composition according to claim 23, wherein each of X and Q is independently selected from the group consisting of -C(O)O-, -O-C(O)-, -C(O)NH-, -NH-C(O)-, -OC(O)NH- and -NHC(O)NH-.

26. (Currently amended) The composition according to claim 16, wherein A is N,  $\text{R}^2$  is benzyl, k, m and  $[[n]]$  are 1, and X is -OC(O)-.



27-29. (cancelled)

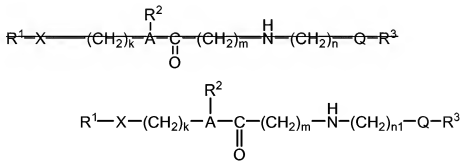
30. (Currently amended) A method for increasing the transport of a biologically active compound across a biological membrane comprising:

administering a composition ~~according to claim 1 comprising a biologically active compound, a transport moiety, and a linker capable of self-immolation linking the biologically active compound and the transport moiety, wherein the transport compound comprises a structure selected from the group consisting of  $(\text{ZYZ})_n\text{Z}$ ,  $(\text{ZY})_n\text{Z}$ ,  $(\text{ZYY})_n\text{Z}$  and  $(\text{ZYYY})_n\text{Z}$ , wherein Z is L-arginine or D-arginine, and wherein Y is an amino acid that does not comprise an amidino or guanidino moiety, and wherein n is an integer ranging from 2 to 10,~~

~~wherein transport of the biologically active biologically active compound across the biological membrane is increased relative to transport of the biologically active compound in the absence of said transport moiety.~~

31. (Canceled).

32. (Currently amended) The method of claim [[31]] 30, wherein the conjugate has the following structure:



wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

A is N or CH<sub>2</sub>;

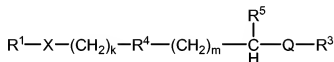
R<sup>2</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>3</sup> is a transport moiety;

k and m are independently either 1 or 2; and

n is an integer of from 1 to 10.

33. (Currently amended) The method of claim [[31]] 30, wherein the conjugate has the following structure:



wherein:

R<sup>1</sup> is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between R<sup>1</sup> and R<sup>3</sup>;

R<sup>2</sup> is a transport moiety;

R<sup>4</sup> is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

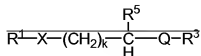
R<sup>5</sup> is OH, SH, NHR<sup>6</sup>, or CONH<sub>2</sub>;

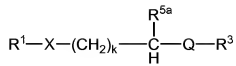
R<sup>6</sup> is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

R<sup>7</sup> and R<sup>8</sup> are independently hydrogen, alkyl or arylalkyl; and

k and m are independently either 1 or 2.

34. (Currently amended) The method of claim [[31]] 30, wherein the conjugate has the following structure:





wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

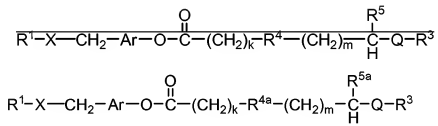
$\text{R}^3$  is the transport moiety;

$\text{R}^{5a}$  is H, OH, SH,  $\text{NHR}^6$ , or  $\text{CONHR}^6$ ;

$\text{R}^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl; and

k is 1 or 2.

35. (Currently amended) The method of claim [[31]] 30, wherein the conjugate is of the following structure:



wherein:

$\text{R}^1$  is the biologically active compound;

X is a linkage between a functional group on the biologically active compound and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Q is a linkage between a functional group on the transport moiety and a functional group on the linker between  $\text{R}^1$  and  $\text{R}^3$ ;

Ar is a substituted or unsubstituted aryl group, wherein the methylene and oxygen substituents are either *ortho* or *para* to one another;

$\text{R}^3$  is the transport moiety;

$R^4$  is S, O, NR<sup>6</sup> or CR<sup>7</sup>R<sup>8</sup>;

$R^5$  is H, OH, SH, CONHR<sup>6</sup> or NHR<sup>6</sup>;

$R^6$  is hydrogen, alkyl, aryl, arylalkyl, acyl or allyl;

$R^7$  and  $R^8$  are independently hydrogen or alkyl; and,

k and m are independently either 1 or 2.

36. (Original) The composition of claim 1, wherein said linker moiety covalently links the biologically active compound and the transport moiety.

37. (Original) The composition of claim 1, wherein said linker moiety capable of self-immolation is configured so as to undergo intramolecular cleavage.

38. (Original) The composition of claim 1, wherein said linker moiety comprises a half-life in the range of between about 10 minutes and about 24 hours in water at 37 °C and at a pH of approximately 7.4.

39. (Canceled).

40. (Canceled).